REMARKS

The Final Office Action mailed December 21, 2005, has been received and reviewed. Claims 37 and 39 are currently pending in the application. Claims 37 and 39 stand rejected. Applicants respectfully request reconsideration of the application.

Power of Attorney (37 C.F.R. 1.34(a)), Revocation of Prior Power of Attorney (37 C.F.R. 1.36) and Request to Change Correspondence Address (37 C.F.R. 1.33 (d)) with Statement Pursuant to 37 C.F.R. 3.73

Applicants' undersigned attorney notes the filing herein of a Power of Attorney (37 C.F.R. 1.34(a)), Revocation of Prior Power of Attorney (37 C.F.R. 1.36) and Request to Change Correspondence Address (37 C.F.R. 1.33 (d)) with Statement Pursuant to 37 C.F.R. 3.73 on September 29, 2005, which filing was not acknowledged in the outstanding Office Action. For the sake of convenience, a second copy of the September 29, 2005, Power of Attorney (37 C.F.R. 1.34(a)), Revocation of Prior Power of Attorney (37 C.F.R. 1.36) and Request to Change Correspondence Address (37 C.F.R. 1.33 (d)) with Statement Pursuant to 37 C.F.R. 3.73 is enclosed herewith.

Supplemental Information Disclosure Statement

Please note that a Supplemental Information Disclosure Statement was filed herein on July 19, 2004, and that no copy of the PTO/SB/08 was returned with the outstanding Office Action. Applicants respectfully request that the information cited on the PTO/SB/08 be made of record herein and that an initialed copy of the PTO/SB/08 evidencing consideration of the cited references be returned to the undersigned attorney. Should the Supplemental Information Disclosure Statement have failed for some reason to have been entered in the Office file, Applicants' undersigned attorney will be happy to have a true copy thereof hand-delivered to the Examiner.

35 U.S.C. § 103(a) Obviousness Rejections

Obviousness Rejection Based on U.S. Patent No. 5,506,268 to Balandrin et al. in view of Drug Facts and Comparisons, 1999 Ed., Pages 1595-1597.

Claim 37 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Balandrin et al. (U.S. Patent No. 5,506,268) in view of Drug Facts and Comparisons, 1999 Ed., Pages 1595-1597. Applicants respectfully traverse this rejection, as hereinafter set forth.

> M.P.E.P. 706.02(j) sets forth the standard for a Section 103(a) rejection:
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> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or combine reference teachings. Second, there must be a reasonable expectation of success. Finally, **the prior art reference (or references when combined) must teach or suggest all the claim limitations.** The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). (Emphasis added).

The obviousness rejection of claim 37 is improper because the cited references do not teach or suggest all of the claim limitations, do not provide a reasonable expectation of success, and do not provide a motivation to produce the claimed invention.

Balandrin teaches using isovaleramide as an anxiolytic or sedative agent in humans. Balandrin at column 1, lines 9-11. Depending on the dose administered, the isovaleramide acts as a mild anxiolytic or mild sedative. *Id.* at column 5, lines 46-48. In addition to its sedative and anxiolytic activity, isovaleramide is administered to hyperexcitable children, premenstrual patients, and substance abuse patients. *Id.* at column 7, lines 25-30. Balandrin also teaches that extracts of valerian have been used as sedatives or antispasmodics. *Id.* at column 1, lines 53-61. Active components of the valerian extracts have not been identified or the effects of the active components characterized. *Id.* at column 2, lines 15-21. Isovaleramide exhibits hypnotic activity when administered to experimental animals in high doses but is not clinically effective as a hypnotic. *Id.* at column 3, lines 3-9. While Balandrin teaches that valproic acid and valpromide are used as antiepileptic agents, Balandrin explicitly states that isovaleramide has no anticonvulsant properties. *Id.* at column 4, lines 60-65. Balandrin also explicitly states "that

there are no clearly discernible structure-function relationships which permit predictability of compounds which will affect the central nervous system in the experimentally distinguishable outcomes described herein below." *Id.* at column 4, line 66 through column 5, line 3.

Drug Facts has been cited for a description of Diazepam, which is indicated as being used for treatment of anxiety disorders and relief of symptoms of anxiety, including treatment of skeletal muscle spasms and status epilepticus. (Office Action at page 2). Drug facts is used "to show that for the purposes of treating the conditions of anxiety disorders, muscle spasms and convulsive disorders such as status epilepticus, one of ordinary skill in the art would have viewed said conditions to be art equivalents" and that "one of ordinary skill in the art would have expected to see therapeutic benefits for treating all such conditions, when any agent is found to be effective to treat any one of said conditions." (*Id.*) (emphasis added)

As amended, claim 37 recites a method of treating convulsions in a patient. The method comprises administering an effective amount of isovaleramide to a patient suffering from a convulsive disorder, wherein the convulsive disorder is selected from the group consisting of simple partial seizures, complex partial seizures, generalized tonic-clonic seizures, secondarily generalized seizures, status epilepticus, and trauma-induced seizures.

The cited references do not teach or suggest the limitation of "administering an effective amount of isovaleramide to a patient suffering from a convulsive disorder, wherein the convulsive disorder is selected from the group consisting of simple partial seizures, complex partial seizures, generalized tonic-clonic seizures, secondarily generalized seizures, status epilepticus, and trauma-induced seizures." As acknowledged by the Examiner, "Balandrin does not specifically teach methods of treating convulsions." Office Action of April 28, 2005, p. 3. Applicants respectfully submit that nothing in Balandrin teaches or suggests administering isovaleramide to a patient suffering from a convulsive disorder. Rather, Balandrin is limited to teaching that isovaleramide is administered as an anxiolytic or sedative. Therefore, Balandrin necessarily does not teach or suggest that the convulsive disorder is selected from the group consisting of simple partial seizures, complex partial seizures, generalized tonic-clonic seizures, secondarily generalized seizures, status epilepticus, and trauma-induced seizures.

As evidence that Balandrin teaches this limitation, the Examiner presents an elaborate argument that attempts to equate spasms with a convulsion. *Id.* at p. 3-4. The Examiner states that "isovaleramide is prepared from extracts of *valeriana officinalis*, which has historically been used as sedative and antispasmodics" and that "the limitation of 'treating convulsions' is viewed to encompass any alleviation that lessens one or more spasms of muscles, including decreasing muscle tone." *Id.* at p. 3. However, contrary to the Examiner's assertions, nothing in Balandrin teaches or suggests that isovaleramide has antispasmodic effects. While Balandrin teaches that valerian extracts have antispasmodic effects, it is improper for the Examiner to rely on this teaching in support of the assertion that isovaleramide has antispasmodic effects, especially since Balandrin teaches that the active components in the valerian extracts have not been identified, nor have the effects of the active components been characterized.

Furthermore, even assuming *arguendo* that the Examiner's argument is correct, the above-mentioned limitation still is not taught or suggested because Balandrin does not teach or suggest that the convulsive disorder is selected from the group consisting of simple partial seizures, complex partial seizures, generalized tonic-clonic seizures, secondarily generalized seizures, status epilepticus, and trauma-induced seizures.

The Examiner also states that Balandrin teaches the administration of isovaleramide to hyperexcitable children, premenstrual patients, and substance abuse patients and relies on this teaching as evidence of isovaleramide's anticonvulsive behavior. *Id.* at p. 3. However, nothing in Balandrin supports the assertion that hyperexcitable children, premenstrual patients, or substance abuse patients have a convulsive disorder selected from the group consisting of simple partial seizures, complex partial seizures, generalized tonic-clonic seizures, secondarily generalized seizures, status epilepticus, and trauma-induced seizures. As such, the Examiner's reliance on isovaleramide being administered to these patients provides no evidence of isovaleramide's anticonvulsive behavior.

With regard to the reliance on Drug Facts, Applicants respectfully disagree with the Examiner's contention that Diazepam, which is a benzodiazepine compound having an entirely different chemical structure than isovaleramide and having a different mechanism of action, somehow provides evidence that treating the conditions of anxiety disorders, muscle spasms and

convulsive disorders such as status epilepticus is viewed by a skilled artisan as being an art equivalent to the conditions recited in claim 37. Applicants also disagree with the contention that one of ordinary skill in the art would have expected to see therapeutic benefits for treating all such conditions, when any agent is found to be effective to treat any one of said conditions. Given the different chemical structure of Diazepam and isovaleramide, as well as the differences in mechanisms of action, such a conclusion is unsupportable.

The cited references also do not provide a reasonable expectation of success. One of ordinary skill in the art would not reasonably expect to treat the recited convulsive disorders by administering isovaleramide to a patient because nothing in the cited references, when combined, provides any teaching or suggestion that isovaleramide would have activity against the recited convulsive disorders. In addition, there is no reasonable expectation of success because Balandrin explicitly teaches that the properties of active components of a valerian extract, such as isovaleramide, are unpredictable, thus, making the disclosure in Drug Facts relating to Diazepam (an unrelated benzodiazepine compound) even further speculative.

In addition, the cited references do not provide a motivation to combine to produce the claimed invention. To provide a motivation or suggestion to combine, the prior art or the knowledge of a person of ordinary skill in the art must "suggest the desirability of the combination" or provide "an objective reason to combine the teachings of the references." M.P.E.P. § 2143.01. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *Id.* (emphasis in original). Applicants respectfully submit that nothing in the cited references, when combined, suggests the desirability of the combination or provides an objective reason to combine. Specifically, nothing in Balandrin suggests the desirability of, or provides an objective reason for, administering isovaleramide to a patient to treat a convulsive disorder, let alone a convulsive disorder selected from the group consisting of simple partial seizures, complex partial seizures, generalized tonic-clonic seizures, secondarily generalized seizures, status epilepticus, and trauma-induced seizures. Drug Facts also does not suggest the desirability of, or provide an objective reason for, administering isovaleramide to a patient to treat the recited

convulsive disorders. Instead, as acknowledged by the Examiner, Drug Facts merely describes use of Diazepam for treating anxiety disorders.

Furthermore, Balandrin teaches away from combination with Drug Facts to produce the claimed invention because Balandrin explicitly teaches that isovaleramide has no anticonvulsant properties. See, Balandrin at column 4, lines 60-65. As such, a person of ordinary skill in the art at the time of the invention, after reading Balandrin and Drug Facts, would not have been motivated to administer isovaleramide to treat a convulsive disorder.

Since the cited references do not teach or suggest all of the claim limitations, do not provide a reasonable expectation of success, and do not provide a motivation to produce the claimed invention, the obviousness rejection of claim 37 is improper and should be withdrawn.

Obviousness Rejection Based on U.S. Patent No. 5,506,268 to Balandrin et al. in view of Pharmacotherapy, A Pathophysiologic Approach (Dipiro et al., 2nd Ed., Elsvier, 1991, Pages 1232, 1238).

Claim 39 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Balandrin et al. (U.S. Patent No. 5,506,268) in view of Pharmacotheraphy, A Pathophysiologic Appropach (Dipiro et al., 2nd Ed., Elsvier, 1991, Pages 1232, 1238) ("Pharmacotherapy"). Applicants respectfully traverse this rejection, as hereinafter set forth.

The obviousness rejection of claim 39 is improper because the cited references do not teach or suggest all of the claim limitations and do not provide a motivation to combine to produce the claimed invention.

The teachings of Balandrin are as previously described.

Pharmacotherapy is "merely used to indicate that headache is a common symptom associated with premenstrual syndrome" and that "antianxiety agents, such as alprazolam, are effective in treating PMS symptoms." (Final Office Action at page 4).

As amended, claim 39 recites a method of treating headaches in a patient. The method comprises administering an effective amount of isovaleramide to a patient suffering from a headache.

The cited references do not teach or suggest all of the limitations of claim 39 because Balandrin and Pharmacotherapy, when combined, do not teach or suggest "administering an effective amount of isovaleramide to a patient suffering from a headache." Balandrin does not teach or suggest this limitation because Balandrin teaches administering isovaleramide as an anxiolytic or sedative. Nothing in Balandrin provides any teaching or suggestion that isovaleramide is useful to treat a headache.

Likewise, reliance on Pharmacotherapy is misplaced. There is no support for the theory that PMS symptoms and headaches are interchangeable or that there is any expectation of success for treating headaches simply because one particular benzodiazepine compound (alprazolam) is effective for treating one or more PMS-related symptoms. Pharmacotherapy recites over 80 symptoms that are associated with PMS. (Pharmacotherapy at page 1232; Table 72.1). It also recites a myriad of therapeutic compounds that have been tried as possible treatments for the numerous symptoms associated with PMS. (*Id.* at pages 1237-1238). The mere listing of numerous possible compounds having potential to treat a myriad of PMS symptoms does not overcome the deficiencies of Balandrin.

The cited references also do not provide a motivation to combine to produce the claimed invention. Nothing in Balandrin and Pharmacotherapy, when combined, suggests the desirability of, or provides an objective reason for, administering an effective amount of isovaleramide to a patient suffering from a headache.

Since the cited references do not teach or suggest all of the claim limitations and do not provide a motivation to produce the claimed invention, the obviousness rejection of claim 39 is improper and should be withdrawn.

CONCLUSION

Claims 37 and 39 are believed to be in condition for allowance, and an early notice thereof is respectfully solicited. Should the Examiner determine that additional issues remain which might be resolved by a telephone conference, the Examiner is respectfully invited to contact Applicants' undersigned attorney.

Respectfully submitted,

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Date: April 21, 2006
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Document in ProLaw